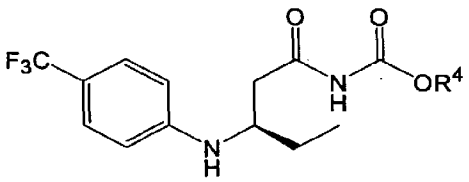
Claim Amendments

Please make the amendments shown below:

1. (Withdrawn) A method for producing an (R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide derivative defined by the following formula (8):

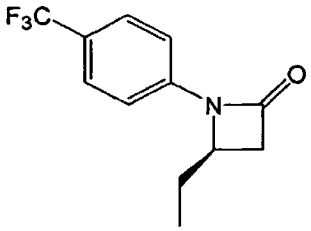


(8)

in the formula, R^4 denotes a C_{1-12} alkyl, a C_{6-12} aryl or a C_{7-12} aralkyl group:

which comprises reacting

(R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone defined by the following formula (2):



(2)

with a carbamic acid ester defined by the following formula (9) :

NH_2COOR^4 (9)

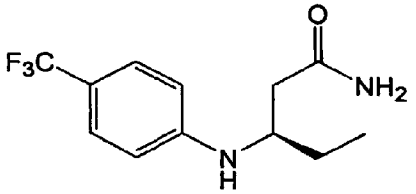
in the formula, R^4 denotes the same described above: in the presence of a base.

2. (Withdrawn) The method according to Claim 1, wherein R^4 is methyl or benzyl group.

3. (Withdrawn) The method according to Claim 1 or 2, wherein the base is sodium hydride, sodium methoxide, sodium ethoxide, sodium isopropoxide, sodium tert-butoxide, potassium tert-butoxide or lithium tert-butoxide.

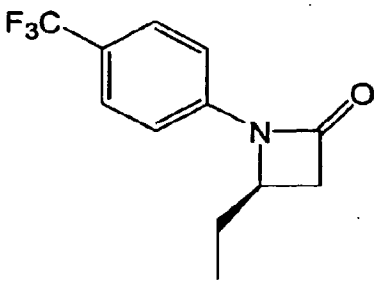
4. (Withdrawn) A method for producing (R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide

defined by the following formula (3):



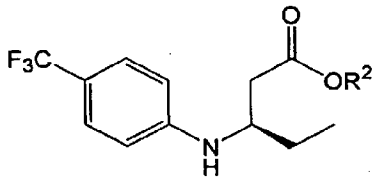
(3)

which comprises i) amidation of (R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone defined by the following formula (2):



(2)

Or ii) amidation of an (R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid derivative defined by the following formula (5):

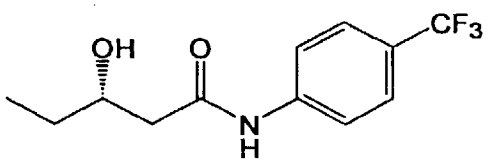


(5)

in the formula, R^2 denotes hydrogen atom or a C_{1-5} alkyl group: obtained by hydrolysis or alcoholysis of the (R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone defined by said formula (2).

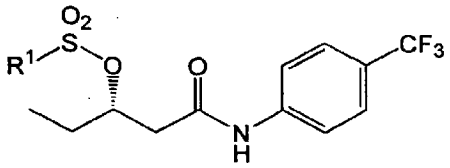
5. (Withdrawn) The method according to Claim 4, wherein R^2 is hydrogen atom, methyl or ethyl group.

6. (Withdrawn) The method according to any one of Claims 1 to 5, wherein the (R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone defined by said formula (2) is produced by l) cyclization of (S)-N-[4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by the following formula (1):



(1)

with a dehydration condensing agent, or ll) a production of an (S)-N-[4-trifluorcimethyl)phenyl]-3-sulfonyloxypentanoic acid amide derivative defined by the following formula (4):



(4)

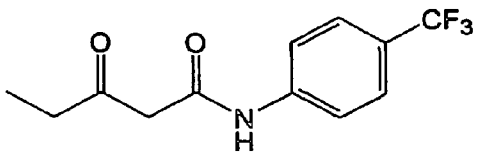
in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent: by sulfonylation of the (S)-N-[4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by said formula (1), and successive treatment with a base.

7. (Withdrawn) The method according to Claim 6, wherein the dehydration condensing agent is a combination of at least one azo compound selected from dimethyl azodicarboxylate, diethyl azodicarboxylate and diisopropyl azodicarboxylate, and at least one phosphine compound selected from tri-n-butylphosphine, tricyclohexylphosphine and triphenylphosphine.

8. (Withdrawn) The method according to Claim 6, wherein R^1 is methyl or 4-methylphenyl group.

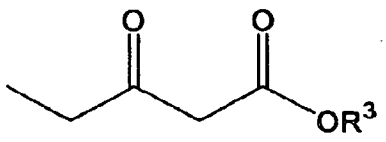
9. (Withdrawn) The method according to Claim 6 or 8, wherein the base is sodium hydride, sodium methoxide, sodium ethoxide, sodium isopropoxide, sodium tert-butoxide, potassium tert-butoxide, lithium tert-butoxide, sodium hydroxide or potassium hydroxide.

10. (Withdrawn) The method according to any one of Claims 6 to 9, wherein the (S)-N-14-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by said formula (1) is produced by asymmetric reduction of N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by the following formula (7):



(7)

11. (Withdrawn) The method according to Claim 10, wherein the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is produced by a reaction of a
3-oxopentanoic acid ester derivative defined by the following formula (6):



(6)

in the formula, R^3 denotes a C_{1-} alkyl group: and 4-(trifluoromethyl)aniline.

12. (Withdrawn) The method according to Claim 11, wherein R^3 is methyl or ethyl group.

13. (Withdrawn) The method according to any one of Claims 10 to 12, wherein the asymmetric reduction of the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is carried out in the presence of an asymmetric transition metal catalyst.

14. (Withdrawn) The method according to Claim 13, wherein the asymmetric transition metal catalyst is ((S) -BINAP) $RuBr_2$, ((S) -BINAP) $RuCl_2$ or $[((S)\text{-BINAP})\ RuCl2]_2NEt_3$, wherein BINAP is 2,2' -bis(diphenylphosphino) -1,1'-binaphthyl).

15. (Withdrawn) The method according to any one of Claims 10 to 12, wherein the asymmetric reduction of the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is carried out by using an enzyme source having activity of stereoselectively reducing the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide.

16. (Withdrawn) The method according to Claim 15, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group consisting of Arthrobacter, Bacillus, Brevibactrium, ClostridiuM, Corynebacterium, Flavobacterium, Luteococcus, Microbacterium, Pseudomonas, Paenibacillus, Serratia, Nocardia, Rathayibacter, Rhodococcus, Candida and Cryptococcus, and/or from the microorganism.

17. (Withdrawn) The method according to Claim 16, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group consisting of Arthrobacter paraffineus, Bacillus cereus, Bacillus subtilis, Bacillus amyloliquefaciens, Bacillus licheniformis, Brevibacterium iodinum, Clostridium cylindrosporum, Corynebacterium flavescens, Corynebacterium xerosis, Flavobacterium flavescens, Luteococcus japonicus, Microbacterium lacticum, Pseudomonas stutzeri, Pseudomonas fluorescens, Paenibacillus amylolyticus, Paenibacillus polymyxa, Paenibacillus alvei, Serratia marcescens, Nocardia globerula, Rathayibacter rathayi, Rhodococcus erythropolis, Candida guilliermondii, Candida intermedia, Candida

molischiana and Cryptococcus albidus, and/or from the microorganism.

18. (Withdrawn) A method for producing an (R)-3-[4-(trifluoromethyl)phenylaminol-pentanoic acid amide derivative defined by said formula (8) which comprises reacting the (R)-3-(4-(trifluoromethyl)phenylamino]-pentanoic acid amide defined by said formula (3) produced by the method according to any one of Claims 4 to 17 with a chlorocarbonic acid ester

defined by the following formula (10):

$$ClCOOR^4 \quad (10)$$

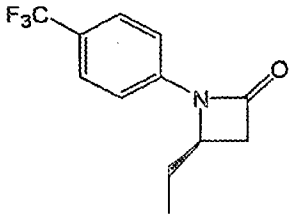
in the formula, R^4 denotes a $C_{1\text{-}12}$ alkyl, a $C_{6\text{-}12}$ aryl or a $C_{7\text{-}12}$ aralkyl group: in the presence of a base.

19. (Withdrawn) The method according to Claim 18, wherein R4 is methyl or benzyl group.

20. (Withdrawn) The method according to Claim 18 or 19, wherein the base is sodium hydride, sodium methoxide, sodium ethoxide, sodium isopropoxide, sodium tert-butoxide, potassium tert-butoxide or lithium tert-butoxide.

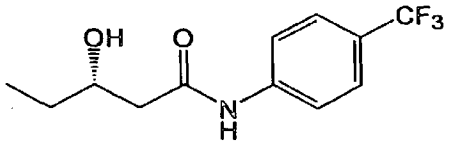
21. (Withdrawn) A method for producing (R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone

defined by the following formula (2):



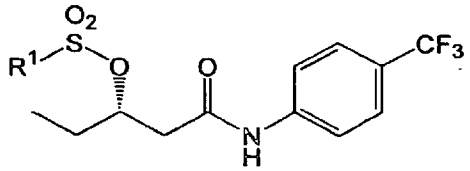
(2)

which comprises I) cyclization of (S)-N-[4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by the following formula (1):



(1)

with a dehydration condensing agent, or II) a production of an (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative defined by the following formula (4):


(4)

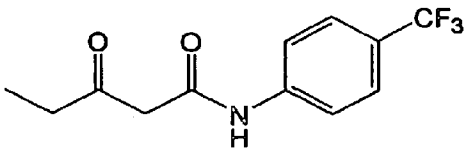
in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent: by sulfonylation of the (S)-N-[4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by said formula (1), and successive treatment with a base.

22. (Withdrawn) The method according to Claim 21, wherein the dehydration condensing agent is a combinationof at least one azo compound selected from dimethylazodicarboxylate, diethyl azodicarboxylate and diisopropyl azodicarboxylate, and at least one phosphine compound selected from tri-n-butylphosphine, tricyclohexylphosphine and triphenylphosphine.

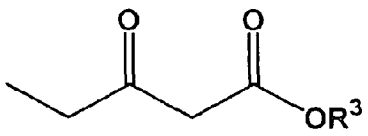
23. (Withdrawn) The method according to Claim 21, wherein R^1 is methyl or 4-methylphenyl group.

24. (Withdrawn) The method according to Claim 21 or 23, wherein the base is sodium hydride, sodium methoxide, sodium ethoxide, sodium isopropoxide, sodium tert-butoxide, potassium tert-butoxide, lithium tert-butoxide, sodium hydroxide or potassium hydroxide.

25. (Withdrawn) The method according to any one of Claims 21 to 24, wherein the (S)-N-(4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by said formula (1) is produced by asymmetric reduction of N-(4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by the following formula (7):


(7)

26. (Withdrawn) The method according to Claim 25, wherein the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is produced by a reaction of a
3-oxopentanoic acid ester derivative defined by the following formula (6):



in the formula, R^3 denotes a C_{1-5} alkyl group: and 4-(trifluoromethyl)aniline.

27. (Withdrawn) The method according to Claim 26, wherein R^3 is methyl or ethyl group.

28. (Withdrawn) The method according to any one of Claims 25 to 27, wherein the asymmetric reduction of the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is carried out in the presence of an asymmetric transition metal catalyst.

29. (Withdrawn) The method according to Claim 28, wherein the asymmetric transition metal catalyst is((S)-BINAP)$RuBr_2$, ((S)-BINAP) $RuCl_2$ or [((S)-BINAP) $RuCl_2]_2NEt_3$, wherein BINAP is
2,2'-bis(diphenylphosphino)-1,1'-binaphthyl).

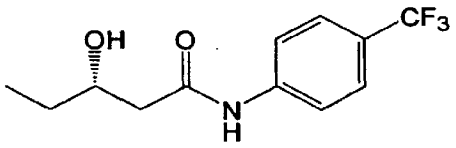
30. (Withdrawn) The method according to any one of Claims 25 to 27, wherein the asymmetric reduction of theN-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide defined by said formula (7) is carried out by using an enzyme source having activity of stereoselectively reducing the N-[4-(trifluoromethyl)pheny1]-3-oxopentanoic acid amide.

31. (Withdrawn) The method according to Claim 30, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group consisting of Arthrobacter, Bacillus, Brevibactrium, Clostridium, Corynebacterium, Flavobacterium, Luteococcus, Microbacterium, Pseudomonas, Paenibacillus, Serratia, Nocardia, Rathayibacter, Rhodococcus, Candida and Cryptococcus, and/or from the microorganism.

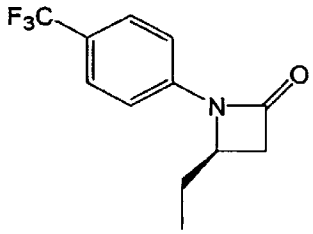
32. (Withdrawn) The method according to Claim 31, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group consisting of Arthrobacter paraffineus, Bacillus cereus, Bacillus subtilis, Bacillus amyloliquefaciens, Bacillus licheniformis, Brevibacterium iodinum, Clostridium cylindrosporum, Corynebacterium flavescens, Corynebacterium xerosis, Flavobacterium flavescens, Luteococcus japonicus, Microbacterium lacticum, Pseudomonas stutzeri, Pseudomonas fluorescens, Paenibacillus amylolyticus, Paenibacillus polymyxa,

Paenibacillus alvei, Serratia marcescens, Nocardia globerula, Rathayibacter rathayi, Rhodococcus erythropolis, Candida guilliermondii, Candida intermedia, Candida molischiana and Cryptococcus albidus, and/or from the microorganism.

33. (Original) (S)-N-[4-(trifluoromethyl)pheny1]-3-hydroxypentanoic acid amide defined by the following formula (1):

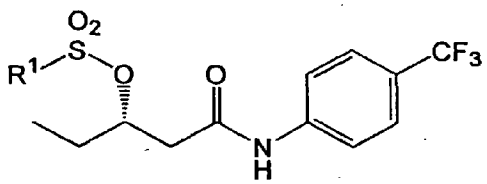


34. (Original) (R)-4-ethy1-1-(4-(trifluoromethyl)phenyl]-2- azetidinone defined by the following formula (2):



(2)

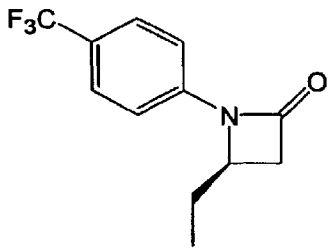
35. (Original) An (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative defined by the following formula (4):



in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent.

36. (Original) The (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative according to Claim 15, wherein R^1 is methyl or 4-methylphenyl group.

37. (Withdrawn) A method for isolating and purifying (R)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone defined by the following formula (2):



(2)

which comprises removing a contaminating (S)-4-ethy1-1-[4-(trifluoromethyl)pheny1]-2-azetidinone by crystallization from a hydrocarbon solvent to obtain the (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone as a crystal with improved optical.purity.

38. (Withdrawn) The method according to Claim 37, wherein the hydrocarbon solvent is hexane, heptane or methylcyclohexane.

39. (Withdrawn) The method according to Claim 37 or 38, wherein the (R)-4-ethy1-1-[4-(trifluoromethyl)phenyl]-2-azetidinone defined by said formula (2) produced by the method according to any one of Claims 21 to 32 is used.

40. (Withdrawn) A method for isolating and purifying an (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative defined by the following formula (4):
in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent: which comprises removing a contaminating (R)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative by crystallization from an aromatic hydrocarbon solvent to obtain an (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative as a crystal with improved optical purity.

41. (Withdrawn) The method according to Claim 40, wherein R^1 is methyl group.

42. (Withdrawn) The method according to Claim 40 or 41, wherein the aromatic hydrocarbon solvent is at least one species selected among benzene, toluene, o-xylene, m-xylene, p-xylene, 1,3,5-mesitylene and cumene.

43. (Withdrawn) The method according to any one of Claims 40 to 42, wherein the (S)-N-[4-(trifluoromethyl)pheny1]-3-sulfonyloxypentanoic acid amide derivative defined by said formula (4) is crystallized by fuither using an auxiliary solvent in order to improve at least one among the yield of the compound (4), the treatment concentration of the compound (4), the liquid property of the compound (4) and the physical property of the crystal to be

obtained.

44. (Withdrawn) The method according to any one of Claims 40 to 43, wherein the auxiliary solvent is at least one species selected among pentane, hexane, heptane, cyclohexane, methylcyclohexane, octane and isooctane.